

Applicant : Coy *et al.*
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REMARKS

Reconsideration of the Instant Office Action, entry of the amendments and new claim and allowance of all pending claims are respectfully requested.

In the instant Office Action, claims 18-43 are listed as pending, claims 18-21, 23 and 32-43 stand rejected and claims 22 and 24-31 have been objected to.

In response to the Instant Office Action, claims 18, 19, 20 and 23 have been amended consistent with the teachings found throughout the specification. New claim 44 has been introduced by way of amendment. No pending claim has been canceled. No amendments of the specification have been requested. Applicants state that said amendments do not introduce new matter and/or do not necessitate any change in inventorship as required under 37 C.F.R. 1.48(b).

1. Claims 18-21 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. In particular, the Examiner states that "[i]n claim 18, substituent "R3" is not specifically defined."

In response thereto, claim 18 has been amended to define R₃ as "OH, NH₂, C₁₋₁₂ alkoxy or NH-Y-CH₂-Z, wherein Y is a C₁₋₁₂ hydrocarbon moiety and Z is H, OH, CO₂H or CONH₂". This definition can be found in original claim 1 which claim 18 was initially dependent thereon when the application was filed. As such, Applicants

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contend that this amendment does not introduce new matter and satisfies the requirements of 35 U.S.C. §112, second paragraph.

Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 18-21 under 35 U.S.C. §112, second paragraph.

2. Claims 18, 19, 20 and 23 stand rejected under 35 U.S.C. §102(b) as anticipated by Coy *et al.*, U.S. Patent 5,462,926 (hereinafter referred to as "the '926 patent").

With respect to the rejection of claim 18, without conceding the correctness of this rejection, Applicants have amended claim 18 and introduced new claim 44 to better distinguish the current application from the cited reference. In particular, claim 18 has been amended to require that R₃ and the carbonyl group of A⁸ be reduced together to form H and lower alkyl or a hydroxyl lower alkyl. Specific embodiments demonstrating this requirement are the compounds of claim 22 all of which terminate in either (2R,3R-(2-hydroxymethyl)-3-hydroxy)propylamide or 2R-(2-naphthyl)ethylamide. As a result of this amendment, A⁸ can no longer be an amino acid, having lost the required carboxyl group. As such, the compounds of claim 18 are now heptapeptides terminating in H, lower alkyl or hydroxyl lower alkyl. In addition, new claim 44, which is a *subgenus* of claim 18 wherein A⁸ is a particular amino acid, i.e., either Thr or β-Nal, and the carboxyl group of said amino acid has been reduced with the R₃ group to produce either a (2R,3R-(2-hydroxymethyl)-3-

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hydroxy)propylamide or a 2R-(2-naphthyl)ethylamide moiety at the C-terminal, respectively, has been added.

The '926 patent is directed to a method of selectively inhibiting the biochemical activity of cells induced by neuromedin β by contacting such cells with particularly identified octapeptides having a terminal amine group ($-\text{NH}_2$). Applicants respectfully submit that the '926 patent does not anticipate the heptapeptides of claim 18 terminating in H, lower alkyl or hydroxyl lower alkyl, and those claims dependent thereon, or the heptapeptides terminating in either (2R,3R-(2-hydroxymethyl)-3-hydroxy)propylamide or 2R-(2-naphthyl)ethylamide of claim 44 and those claims dependent thereon.

With respect to claim 23, without conceding the correctness of this rejection, claim 23 has been amended to restrict A² to a D-aromatic amino acid. This amendment is consistent with the preferred embodiments listed in claim 27 all of which have either D-Phe or D-Cpa in the 2nd position. Both D-Phe and D-Cpa have a benzyl group as part of their side chains. This restriction produces linear octapeptides.

All of the compounds employed in the method taught by the '926 patent all have D- or L-Cys, an aliphatic amino acid, in the 2nd position.

The Court of Appeals for the Federal Circuit, in ruling on the standard for anticipation under 35 U.S.C. §102(b), has stated that

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"[i]t is elementary that an anticipation rejection requires a showing that *each limitation* of a claim must be found in a single reference, practice, or device."

In re Donohue, 226 U.S.P.Q. 619 (1985) (*emphasis added*); and has further stated that

"... exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference",

Atlas Power Co. v. E. I. duPont DeNemours & Co., 224 U.S.P.Q. 409, 411 (1984).

Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of claims 18, 19, 20 and 23 under 35 U.S.C. §102 (b) as anticipated by Coy *et al.*, U.S. Patent 5,462,926.

3. Claims 18, 19, 20, 23 and 32-43 stand rejected under 35 U.S.C. §102(e) as anticipated by Bass *et al.*, U.S. Patent 5,846,934 (hereinafter referred to as "the '934 patent").

Applicants adopt as if re-alleged in its entirety herein, the above argument with respect to the rejection based on the '926 patent. Applicants allege that the '934 patent can not support a rejection under 35 U.S.C. §102(e) since it is directed to cyclic octapeptides have a terminal amine. As stated previously, amended claim 18 and those claims dependent thereon, are all directed to heptapeptides terminating in H, a lower alkyl or a hydroxyl lower alkyl and amended claim 23 and the claims dependent thereon, are all directed to linear octapeptides having an aromatic amino acid in the 2nd position in the sequence. The '934 patent is directed

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to a method of decreasing the effect of somatostatin by administering an amine-terminating cyclic octapeptide. Since the '934 patent does not disclose either a heptapeptide terminating in H, a lower alkyl or a hydroxyl lower alkyl or a linear octapeptide having an aromatic amino acid in the 2nd position, it can not anticipate the claims of the current application.

Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of claims 18, 19, 20, 23 and 32-43 under 35 U.S.C. §102(e) as anticipated by Bass *et al.*, U.S. Patent 5,846,934.

4. Claims 18, 19, 23, 24, 25, 36 and 42 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Coy *et al.*, U.S. Patent 5,597,894 (hereinafter the '894 patent") in view of Bass *et al.*, Molecular Pharmacology, (1996), 4(50):709-715 (hereinafter referred to as the "Bass article"). In support of the rejection, the Examiner first identified two compounds from the '894 patent, D-B-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr(NH₂) and D-Tyr-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂ used for identifying somatostatin-receptor expressing tumors. The Examiner then goes on to argue that the Bass article teaches the use of a somatostatin antagonist containing a core structure having a D,L-Cys at either the 2nd or 7th positions. In summation, the Examiner opines that "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the analogs of Coy *et al.* to have a D-Cys at position 2 because Bass

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et al. teach that somatostatin analogs with D-Cys(2) and L-Cys(7) display potent antagonist properties."

Without conceding the correctness or the merits of the Examiner's reasoning, Applicants take the position that the proposed amendments of claims 18 and 23 render the Examiner's reasons for this rejection moot. Without specifically addressing the teachings of either the '894 patent or the Bass article, Applicants note that claim 18 is now directed to heptapeptides terminating in either H, a lower alkyl or a hydroxyl lower alkyl, which are not analogous to the two Coy compounds, i.e., D-B-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr(NH₂) and D-Tyr-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂, and that claim 23 has been amended to exclude aliphatic amino acids, like D- or L-Cys from the 2nd position. As such, based on the Examiner's reasoning, neither the '894 patent nor the Bass article is relevant with respect to amended claims 18 and/or 23. Accordingly, the 35 U.S.C. §103(a) rejection is no longer supported.

Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of claims 18, 19, 23, 24, 25, 36 and under 35 U.S.C. §103(a) as unpatentable over Coy et al, U.S. Patent 5,597,894 in view of Bass et al., Molecular Pharmacology, (1996), 4(50):709-715.

5. Applicants are grateful for the conditional allowance of claims 22 and 24-31. Applicants, however, have declined the Examiner's invitation to amend these claims in independent form,

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including all of the limitations of the base claim and any intervening claims, in anticipation that base claims 18 and 23 have been successfully amended to overcome the rejections thereof. Applicants respectfully request a subsequent opportunity to amend claims 22 and 24-31, as offered by the examiner, if either one of the rejections of amended claims 18 or 23 is maintained.

CONCLUSION

Applicants submit that each ground for rejection asserted by the Examiner in the instant Office Action has been removed. On this basis, it is submitted that claims 18-44 are now in a condition for allowance.

Prompt and favorable action is solicited.

Should Examiner Delacroix-Muirheid deem that any further action be desirable with respect to these matters, she is requested to telephone the Applicants' undersigned representative.

The Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any

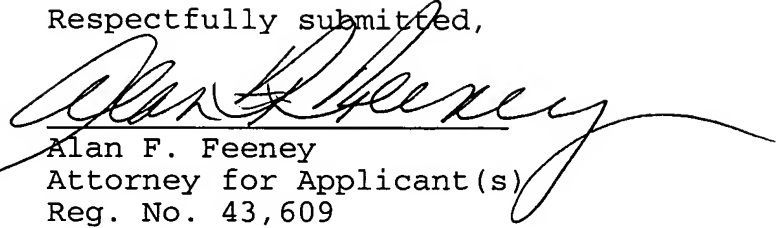
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Respectfully submitted,


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